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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/358,141	07/20/1999	JEFFREY R. SAMPSON	10990393-1	1170

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AGILENT TECHNOLOGIES, INC.
INTELLECTUAL PROPERTY ADMINISTRATION, LEGAL DEPT.
P.O. BOX 7599
M/S DL429
LOVELAND, CO 80537-0599

EXAMINER	
ZARA, JANE J	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 12/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/358,141	**Applicant(s)** SAMPSON, JEFFREY R.	
	Examiner Jane Zara	**Art Unit** 1635	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 August 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): obviousness double patenting (provisional).
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1 and 25-35*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☒ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: please see attachment.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

Attachment

Claims 1 and 25-34 are rejected under 35 U.S.C. 102(e) as being anticipated by Vivekananda et al for the reasons of record set forth in the Office actions mailed 12-17-03 and 6-7-05.

Applicant's arguments filed 8-15-05 have been fully considered but they are not fully persuasive. Applicants argue that Vivekananda et al does not properly anticipate the claimed invention because Vivekananda et al do not teach methods of synthesizing nucleic acid molecules with reduced secondary structure, but instead disclose describe their nucleic acids as aptemers, and utilize nucleic acid molecules that are able to specifically bind particular targets including through non-Watson-Crick interactions. Applicants argue further that Vivekananda et al define preferred nucleic acid aptamers as nucleic acids that bind to other molecules which do not encompass standard nucleic acid hydrogen bond formation exemplified by Watson-Crick base pair formation, but instead encompass all other types of non-covalent binding. Applicants are correct that Vivekananda et al teach aptamers as a preferred embodiment. But, contrary to Applicants' assertions, the fact that aptamers are a preferred embodiment does not preclude Vivekananda as prior art of the instantly claimed invention. Applicant argues that Vivekananda does not teach an unstructured nucleic acid in which two complementary nucleotides of the unstructured nucleic acid do not form an intramolecular base pair. In columns 20-24, 29-31, Vivekananda et al teach the synthesis of nucleic acid ligands that contain modified nucleotides that render intra-strand, complementary nucleotides with a reduced ability to form stable hydrogen bonded base pairs. So, contrary to Applicant's assertions, Vivekananda et al specifically disclose the incorporation of 2'-amino purines, 2'-thio substituted bases including

2'-thio cytodine and 2'-thio uridine, as well as the incorporation of inosine into nucleic acid ligands through various methods including PCR, RT-PCR, LCR, and several other nucleic acid amplification procedures. Vivekananda et al nevertheless teach the instantly claimed methods of synthesizing nucleic acid polynucleotides with reduced secondary structure by incorporating the claimed modified bases, thereby producing nucleic acid strands with a reduced ability to form intra-molecular base pairs.

Claims 1 and 25-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Kutyavin et al for the reasons of record set forth in the Office actions mailed 12-17-03 and 6-7-05.

Applicant's arguments filed 8-15-05 have been fully considered but they are not persuasive. Applicants argue that Kutyavin et al is not proper prior art because they teach methods of producing polynucleotides with reduced ability to form inter-molecular base pairs, as opposed to the instantly claimed invention which teaches a method of producing polynucleotides with reduced ability to form intra-molecular base pairs. Applicant argues that not all steps/features of the claimed invention are taught or suggested by Kuytavin because the instant claims have an embodiment that includes providing a nucleic acid template and providing nucleotides that have certain characteristics such that when the nucleotides are polymerized to form an unstructures nucleic acid, the nucleotides do not form an intramolecular base pair. Contrary to Applicant's assertions, Kuyativin et al does disclose methods of synthesizing polynucleotides with a reduced ability to form self annealing double strands by incorporating the modified bases claimed, which in turn renders the polynucleotides with reduced ability to form stable hydrogen bonded base pairs with either a complementary strand or with complementary

bases within the same strand (see e.g. col. 1 of Kutyavin et al: "[t]he ODNs include modified bases of such nature that the modified base forms stable hydrogen bonded base pairs with the natural partner base, but does not form stable hydrogen bonded base pairs with its modified partner... The ODNs of the invention, however, form substantially stable hybrids with the target sequence in each strand of duplex nucleic acid."). The procedure disclosed by Kutyavin, therefore, is indistinguishable from the instantly claimed methods because they both involve the synthesis of oligonucleotides in the presence of modified bases to produce nucleic acid with reduced ability to hybridize to complementary bases by reducing the ability to form Watson-Crick base pairing. This characteristic exists in intra-molecular as well as inter-molecular, complementary nucleic acid strands. Kuyativin et al properly anticipates the instantly claimed methods. The distinction between inter-molecular and intra-molecular base complementarity that is repeatedly stressed by Applicant to distinguish the instantly claimed invention from the prior art is also addressed by Kutyavin et al, albeit within the context of the target sequence: "It is known that secondary structure of mRNA and ribosomal RNA do not have two strands in the strict sense of that term. Nevertheless, unless the context otherwise indicates, in the present description the terminology "two strands" of double stranded nucleic acids also refers to the two complementary portions of duplex mRNA or of duplex ribosomal RNA as well. The general concept of double stranded DNA and of secondary structure ... is covered in this description by the term "duplex nuclei acid." (see col. 4). For these reasons, the instant 102 rejections are maintained.

For these reasons the prior art rejections are maintained.

SEAN McGARRY
PRIMARY EXAMINER
1635